

National Stage of International Appln. No.: PCT/US98/02007
KÖSTER et al.
PRELIMINARY AMENDMENT

IN THE CLAIMS:

Please cancel claim 52 without prejudice or disclaimer.

Please add claims 53-56 as follows:

- but C4*
- 53. The insoluble support of claim 16, wherein the polypeptide is an enzyme.—
- 54. The insoluble support of claim 53, wherein the enzyme is an alkaline phosphatase.—
- 55. The insoluble support of claim 54, wherein the enzyme is bacterial alkaline phosphatase (BAP).—
- 56. The insoluble support of claim 1, wherein the reversible linkages are different.—

Please amend claims 1-36, 40, 41 and 44-51 as follows:

- 3*
but C1
1. (Amended) [A composition comprised of at least] An insoluble support, comprising two biopolymers, [conjugated to an insoluble support by at least one reversible linkage] wherein:
the first biopolymer is linked to the support by a reversible linkage; and
the second biopolymer is linked to the first biopolymer by a reversible linkage.
2. (Amended) [A composition according to] The insoluble support of claim 1, wherein the [at least] two biopolymers are comprised of nucleic acids.
3. (Amended) [A composition according to] The insoluble support of claim 1, wherein the [at least] two biopolymers are comprised of polypeptides.
4. (Amended) [A composition according to] The insoluble support of claim 1, wherein the [at least] two biopolymers are comprised of a nucleic acid and a protein.
5. (Amended) [A composition according to] The insoluble support of claim 1, wherein [the at least] one reversible linkage is formed through a trityl derivative, a chelate complex, a hydrophobic interaction or a photocleavable functionality.

National Stage of International Appln. No.: PCT/US98/02007
KÖSTER et al.
PRELIMINARY AMENDMENT

6. (Amended) [A composition according to] The insoluble support of claim 1, wherein the insoluble support is selected from the group consisting of[:] a flat surface, a microtiter plate, a comb and a bead.

7. (Amended) [A composition according to] The insoluble support of claim 6, wherein the insoluble support is selected from the group consisting of[:] a silicon wafer, glass plate, metal, plastic, film and composites thereof with pits or wells.

8. (Amended) [A composition according to] The insoluble support of claim 7, further comprising two or more additional linked biopolymers, wherein the [biopolymer is conjugated] biopolymers are linked to the insoluble support in an array format.

9. (Amended) [A composition according to] The insoluble support of claim 7, wherein the [bead is comprised of] support comprises an inorganic material selected from the group consisting of[:] silica, Controlled Pore Glass (CPG), plastic, metal, cellulose, [Sephacrose and Sephadex] agarose and dextran cross-linked with epichlorohydrin.

10. (Amended) [A composition according to] The insoluble support of claim 6, wherein the insoluble support [is comprised of] comprises a magnetic or electromagnetic material.

11. (Amended) [A composition according to] The insoluble support of claim 2, wherein the nucleic [acid is] acids are selected from the group consisting of[:] deoxyribonucleic acid (DNA), ribonucleic acid (RNA) [or] and analogs or mimetics of DNA or RNA.

12. (Amended) [A composition according to] The insoluble support of claim 3, wherein the [polypeptide is] polypeptides are selected from the group consisting of an antibody, enzyme, receptor [or] and peptide.

National Stage of International Appln. No.: PCT/US98/02007
KÖSTER et al.
PRELIMINARY AMENDMENT

sub C1 13. (Amended) [A composition according to] The insoluble support of claim 1, [which contains] further comprising a spacer between the first biopolymer and the insoluble support.

14. (Amended) [A composition according to] The insoluble support of claim 4, [which is made by the formation of a chelate complex between the nucleic acid and the polypeptide] wherein the reversible linkage between the nucleic acid and the polypeptide comprises a chelate complex.

15. (Amended) [A composition according to] The insoluble support of claim 14, wherein the chelate complex is formed by the reaction of a nucleic acid containing a chelate functionality with a polypeptide containing an [imidazolyl] imidazolyl functionality in the presence of a metal ion.

16. (Amended) [A composition] The insoluble support of claim 14, wherein the chelate complex is formed by the reaction of a nucleic acid containing an [imidazolyl] imidazolyl functionality with a polypeptide containing a chelate functionality in the presence of a metal ion.

17. (Amended) [A composition according to] The insoluble support of claim 15 [or 16], wherein the polypeptide is an enzyme.

18. (Amended) [A composition according to] The insoluble support of claim 17, wherein the enzyme is an alkaline phosphatase.

19. (Amended) [A method according to] The insoluble support of claim 18, wherein the enzyme is bacterial alkaline phosphatase (BAP).

20. (Amended) A method for [making a composition] preparing the insoluble support of claim 1, comprising the steps of:

a) immobilizing a nucleic acid to an insoluble support via a first reversible linkage; and

b) conjugating said nucleic acid with a polypeptide via a second reversible linkage.

National Stage of International Appln. No.: PCT/US98/02007
KÖSTER et al.
PRELIMINARY AMENDMENT

21. (Amended) [A method according to] The method of claim 20, wherein the first or second reversible linkage is formed through a trityl derivative, a chelate complex, a hydrophobic interaction or a photocleavable functionality.

22. (Amended) A method according to claim 20, wherein in step b), the [first or] second reversible linkage forms a chelate complex.

23. (Amended) [A method according to] The method of claim 22, wherein the first or second reversible linkage is formed by the reaction of a nucleic acid containing a chelate functionality with a polypeptide containing an [imidazolyl] imidazolyl functionality in the presence of a metal ion.

24. (Amended) [A method according to] The method of claim 22, wherein the first or second reversible linkage is formed by the reaction of a nucleic acid containing an [imidazolyl] imidazolyl functionality with a polypeptide containing a chelate functionality in the presence of a metal ion.

25. (Amended) [A method according to] The method of claim 20, wherein the first or second reversible linkage [are] is formed from functionalities or precursors, which are introduced into the nucleic acid during enzymatic synthesis.

26. (Amended) [A method according to] The method of claim 25, wherein the enzymatic synthesis is part of an amplification procedure.

27. (Amended) [A] The method of claim 26, wherein the amplification procedure is selected from the group consisting of the polymerase chain reaction (PCR), the ligase chain reaction (LCR) and strand displacement amplification (SDA).[.]

28. (Amended) [A method according to] The method of claim 25, wherein the enzymatic synthesis is part of a nucleic acid sequencing procedure.

National Stage of International Appln. No.: PCT/US98/02007
KÖSTER et al.
PRELIMINARY AMENDMENT

29. (Amended) An oligonucleotide analog [comprised of] comprising a β -cyanoethylphosphoamidite functionality [with] linked to a chelate functionality.

30. (Amended) [An] The oligonucleotide analog of claim 29, wherein the chelate functionality is a precursor of nitrilotriacetic acid derived from [either] serine, cysteine or lysine.

31. (Amended) An oligonucleotide analog, [comprised of] comprising a heterobifunctional trityl group [with] linked to a chelate functionality.

32. (Amended) [An] The oligonucleotide analog of claim 31, wherein the chelate functionality is a precursor of [nitrilotrisacetic] nitrilotriacetic acid derived from serine, cysteine or lysine.

33. (Amended) An oligonucleotide analog, [comprised of] comprising a β -cyanoethylphosphoamidite functionality [with] linked to an imidazolyl functionality.

34. (Amended) An oligonucleotide analog, [comprised of] comprising a heterobifunctional trityl group [with] linked to [a] an oligohistidyl or oligoimidazolyl sequence.

35. (Amended) [An] The oligonucleotide analog [according to] of claim 34, wherein the oligohistidyl sequence is present at the 5'- or 3'- terminus.

36. (Amended) An oligonucleotide analog, [comprised of] comprising an imidazolynucleoside- β -cyanoethylphosphoamidite.

40. (Amended) [A] The recombinant protein [according to] of claim 39 which has enzymatic activity.

41. (Amended) [A] The recombinant protein [according to] of claim 40, which is an alkaline phosphatase that comprises [, which has] an alanine residue at its N-terminus instead of arginine-threonine and [which has] at its C-terminus a chain of [six] histidine residues.

ent C2
44. (Amended) [A composition] The insoluble support of claim 1,
wherein:

B6
the first biopolymer is a nucleic acid;

the insoluble support is linked via a spacer to the nucleic acid through a
reversible heterobifunctional trityl group;

the second biopolymer is an enzyme; and

the nucleic acid is conjugated to [an] the enzyme through a reversible
chelate [functionality] complex.

45. (Amended) [A composition according to] The insoluble support of
claim 44 in which the [polymer] insoluble support is comprised of magnetic
beads[,] ; the chelate complex is formed via [the] a nitrilotriacetic acid
functionality in the presence of Ni^{2+} ; and the enzyme is BAP-his₆.

46. (Amended) [A composition according to] The insoluble support
claim 44 in which the [polymer] insoluble support is a silicon wafer carrying the
reversible functionalities to bind the nucleic acid either directly on the surface or
through beads in pits or wells in an array format[,] ; the chelate complex is
formed via [nitrilotrisacetic] a nitrilotriacetic acid functionality in the presence of
 Ni^{2+} ; and the enzyme is BAP-his₆.

47. (Amended) [A composition according to] The insoluble support of
claim 44 in which the [polymer] insoluble support is the filter bottom in the wells
of a microtiter filter plate[,] ; the chelate complex is formed via [nitrilotrisacetic] a
nitrilotriacetic acid functionality in the presence of Ni^{2+} ; and the enzyme [if] is
BAP-his₆.

48. (Amended) A method of purification, comprising:
[of using the composition according to] contacting the insoluble support of
claim 44[to] with [purify and to detect] products of nucleic acid amplification
procedures, whereby the products are purified.

National Stage of International Appln. No.: PCT/US98/02007
KÖSTER et al.
PRELIMINARY AMENDMENT

49. (Amended) [A] The method of claim 48, wherein the amplification procedure is selected from the group consisting of[:] the polymerase chain reaction, the ligase chain reaction and strand displacement amplification.

50. (Amended) A method of sequencing a target nucleic acid, [for using the composition according to] comprising sequencing target nucleic acid wherein nucleic acid bound to the insoluble support of claim 44 serves as a primer[for determining the sequence of a nucleic acid].

51. (Amended) A method for genetic or expression profiling, comprising [for using the composition according to] contacting the insoluble support of claim 44 with a sample comprising mRNA or cDNA, thereby detecting [to purify and to detect] the identity and relative quantity of the mRNA or cDNA [mRNAs or their corresponding cDNAs for genetic or expression profiling].

REMARKS

Claims 1-51 and 53-56 are presently pending. Claims 1-36, 40, 41 and 44-51 are amended herein. The claims are amended herein to delete multiple dependencies, to ensure proper dependency, and to correct obvious typographical and other obvious errors. Basis for the amendment to claim 1 herein may be found in the specification, for example, at page 5, line 11 through page 7, line 24, and in Figures 1-3.

Claim 52 is cancelled herein without prejudice or disclaimer. Applicant reserves the right to file divisional applications to any cancelled subject matter.

Claim 9 is amended to remove trademarks, and to replace them with their generic equivalents.

Similarly, the specification is amended to identify trademark items as such (e.g., Sephadex and Sepharose represented as Sephadex^R and Sepharose^R, respectively), and to provide generic equivalents for trademark items (Sephadex^R and Sepharose^R) on page 5, line 24. These items are well-known to individuals skilled in the art and their generic descriptions are readily available. Pages from